

Amendments to the Claims

The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Withdrawn) A method of killing cancer cells, comprising administration to said cells of an effective amount of a c-FLIP inhibitor, wherein the c-FLIP inhibitor is administered as the sole cytotoxic agent in the substantial absence of other cytotoxic agents.
2. (Withdrawn) A method of treating cancer comprising administration to a subject in need thereof a therapeutically effective amount of a c-FLIP inhibitor, wherein the c-FLIP inhibitor is administered as the sole cytotoxic agent in the substantial absence of other cytotoxic agents.
3. (Withdrawn) A method of killing cancer cells having a p53 mutation, comprising administration to said cells of:
 - (a) a c-FLIP inhibitor and
 - (b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, oxaliplatin or a topoisomerase inhibitor.
4. (Withdrawn) A method of treating cancer associated with a p53 mutation comprising administration to a subject in need thereof
 - (a) a c-FLIP inhibitor and
 - (b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, oxaliplatin or a topoisomerase inhibitor.
5. (Withdrawn) The method according to claim 3, further comprising administration of:
 - (c) a death receptor binding member.

6. (Withdrawn) The method according to claim 5, wherein the death receptor is FAS.
7. (Withdrawn) The method according to claim 6, wherein the binding member is the FAS antibody CH11.
8. (Withdrawn) The method according to claim 3, wherein the chemotherapeutic agent is 5-FU, oxaliplatin or CPT-11.
9. (Withdrawn) The method according to claim 8, wherein the chemotherapeutic agent is 5-FU or oxaliplatin.
10. (Withdrawn) The method according to claim 4, wherein the c-FLIP inhibitor and the chemotherapeutic agent are administered in a potentiating ratio.
11. (Withdrawn) The method according to claim 10, wherein the c-FLIP inhibitor and the chemotherapeutic agent are administered in concentrations sufficient to produce a CI of less than 0.85.
12. (Withdrawn) The method according to claim 4, wherein the p53 mutation is such that p53 is completely inactivated in the cancer cells.
13. (Withdrawn) The method according to claim 4, wherein the p53 mutation is a missense mutation resulting in the substitution of histidine (R175H mutation) or a missense mutation resulting in the substitution of tryptophan (R248W mutation) for arginine.
14. (Withdrawn) The method according to claim 2, wherein said c-FLIP inhibitor is an RNAi agent, which modulates expression of a c-FLIP gene.

15. (Withdrawn) The method according to claim 14 wherein the c-FLIP inhibitor is an RNAi agent having nucleotide sequence

AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or
AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

16.-28. (Cancelled)

29. (Withdrawn) A pharmaceutical composition for the treatment of cancer, wherein the composition comprises a c-FLIP inhibitor as the sole cytotoxic agent and a pharmaceutically acceptable excipient, diluent or carrier, wherein the composition is for treatment in the absence of other cytotoxic agents.

30. (Currently amended) A pharmaceutical composition for the treatment of a cancer associated with a p53 mutation, wherein the composition consists of ~~comprises~~

- (a) a c-FLIP inhibitor which is an antisense or RNAi agent,
- (b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, ~~oxaliplatin~~ or a topoisomerase I inhibitor, and
- (c) optionally, when the chemotherapeutic agent is a topoisomerase I inhibitor, a death receptor binding member, and
- (d) ~~(e)~~ a pharmaceutically acceptable excipient, diluent or carrier.

31. (Cancelled).

32. (Currently amended) The composition according to claim 30 ~~31~~, wherein the death receptor binding member when the chemotherapeutic agent is a topoisomerase I inhibitor is a binding member that binds the death receptor is FAS.

33. (Currently amended) The composition according to claim 32, wherein the death receptor binding member is the FAS antibody CH11.

34. (Currently amended) The composition according to claim 30, wherein the chemotherapeutic agent is 5-FU, ~~oxaliplatin~~ or CPT-11.
35. (Currently amended) The composition according to claim 34, wherein the chemotherapeutic agent is 5-FU ~~or oxaliplatin~~.
36. (Previously Presented) The composition according to claim 30, wherein the c-FLIP inhibitor and the chemotherapeutic agent are present in a potentiating ratio.
37. (Original) The composition according to claim 36, wherein the c-FLIP inhibitor and the chemotherapeutic agent are present in concentrations sufficient to produce a CI of less than 0.85.
38. (Previously Presented) The composition according claim 30, wherein the p53 mutation is such that p53 is completely inactivated in the cancer cells.
39. (Previously Presented) The composition according to claim 30, wherein the p53 mutation is a missense mutation resulting in the substitution of histidine (R175H mutation) or a missense mutation resulting in the substitution of tryptophan (R248W mutation) for arginine.
40. (Withdrawn) The composition according to claim 29, wherein said c-FLIP inhibitor is an RNAi agent, which modulates expression of a c-FLIP gene.
41. (Withdrawn) The composition according to claim 40 wherein the c-FLIP inhibitor is an RNAi agent having nucleotide sequence
AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or
AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

42. (Currently amended) A kit for the treatment of cancer associated with a p53 mutation, said kit consisting of comprising

- (a) a c-FLIP inhibitor and
- (b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, ~~oxaliplatin~~ or a topoisomerase I inhibitor, ~~and~~
- (c) optionally, when the chemotherapeutic agent is a topoisomerase I inhibitor, a death receptor binding member, and
- ~~(e)~~ (d) instructions for the administration of (a) and (b) separately, sequentially or simultaneously.

43. (Original) An RNAi agent having nucleotide sequence
AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or
AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

44. (Original) An RNAi agent consisting of nucleotide sequence
AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or
AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

45. (Withdrawn) The method according to claim 4, wherein said c-FLIP inhibitor is an RNAi agent, which modulates expression of a c-FLIP gene.

46. (Withdrawn) The method according to claim 45, wherein the c-FLIP inhibitor is an RNAi agent having nucleotide sequence
AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or
AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

47. (Previously Presented) The composition according to claim 30, wherein said c-FLIP inhibitor is an RNAi agent, which modulates expression of a c-FLIP gene.

48. (Previously Presented) The composition according to claim 47, wherein the c-FLIP inhibitor is an RNAi agent having nucleotide sequence

AAG CAG TCT GTT CAA GGA GCA (SEQ ID NO: 1) or

AAG GAA CAG CTT GGC GCT CAA (SEQ ID NO: 2).

49. (Currently amended) ~~The composition according to claim 30,~~ A pharmaceutical composition for the treatment of a cancer associated with a p53 mutation, wherein the composition comprises:

(a) a c-FLIP inhibitor, wherein said c-FLIP inhibitor is an antisense or RNAi agent,

(b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor or a topoisomerase I inhibitor and

(c) a pharmaceutically acceptable diluent or carrier,

wherein the composition does not comprise a death receptor binding member, or a nucleic acid encoding said binding member.

50. (Previously presented) The composition according to claim 49, wherein said c-FLIP inhibitor and said chemotherapeutic agent are the sole active agents in said composition.

51. (Currently amended) ~~The kit according to claim 42,~~ A kit for the treatment of cancer associated with a p53 mutation, said kit comprising

(a) a c-FLIP inhibitor and

(b) a chemotherapeutic agent, wherein the chemotherapeutic agent is a thymidylate synthase inhibitor, or a topoisomerase I inhibitor and

(c) instructions for the administration of (a) and (b) separately, sequentially or simultaneously,

wherein the kit does not comprise a death receptor binding member, or a nucleic acid encoding said binding member.

52. (Previously presented) The kit according to claim 51, wherein said c-FLIP inhibitor and said chemotherapeutic agent are the sole active agents in said kit.